

ing characteristics of coronary embolism from the angina pectoris of the ordinary form "the flutter and lability of the heart, the rapid, irregular, and failing pulse, the waning sounds, the dyspnea, and the cyanosis." He as well as Hochhaus<sup>5</sup> and Ohrastow and Streschesko<sup>6</sup> refer to the fact that the pain in infarction of the heart is more continuous than in typical angina. The 4 cases of coronary thromboses reported by Hochhaus all had typical precordial anginal pain with no evidence of an acute inflammatory process. The cases here presented had the further perplexing factors of a leukocytosis and fever. In the second of our 2 cases a definite diagnosis of infarction of the heart was made ante-mortem when the complete heart-block developed. It was only retrospectively that the cardiac factor in the above 2 cases was appreciated, for in the first there was precordial pain on exertion for a year and in the second dyspnea on exertion for the same length of time.

**CONCLUSION.** Two cases are here presented which gave the history and presented the signs of an acute inflammatory or perforative lesion of the upper abdomen, but turned out to have coronary thrombosis with infarction of the heart.

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## A BRIEF EXPERIMENTAL STUDY OF THE MORPHOLOGY OF THE HEART MUSCLE FOLLOWING HYPOTHYROIDISM.<sup>1</sup>

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SLOW action of the heart is one of the chief characteristic features of hypothyroidism whether occasional or continuous, spontaneous or operative. In some cases other aspects of the heart action give also the appearance of a myocardial disease. Thus exercise, though followed by dyspnea, may not be accompanied by commensurate increase in heart rate. The quality and vigor of the heart muscle tone is often greatly impaired and the valve closures are no longer clear and prompt. The capillary return, particularly in the periphery is delayed, favoring fibrosis and diminishing parenchymatous activity.

The use of digitalis, camphor, caffeine, and similar drugs in most of these instances fails to improve these symptoms, but even in

<sup>5</sup> Deutsch. med. Wehnschr., 1911, No. 2, p. 2065.

<sup>6</sup> Ztsch. f. klin. Med., 1910, lxxi, 116.

<sup>1</sup> Read at the meeting of the Association of American Physicians, 1917.

long-standing cases, the giving of thyroid quickly relieves in large part inadequate heart action or now renders the action of the drugs effective.

A diagnosis of myocarditis, or more probably of myocardial degeneration, would be a very natural conclusion in such instances were it not for the other signs of thyroid deficiency and the prompt relief of this among the other signs and symptoms of a defect which follows when thyroid is given.

Inasmuch as these cardiac signs appear quite early in hypothyroidism it is to be expected that whatever the basic cause be, it should become evident in the heart mechanism fairly soon. If the changes induced were of an anatomical nature, relief of any rapid degree in long standing examples would not be expected following thyroid medication. In cases which give histories of thyroid instability, especially such as had at some time shown definite hypothyroidism, permanent signs and symptoms of muscle defect may, however, appear.

It is obvious that this question cannot be satisfactorily answered by the study of material taken from clinical cases of hypothyroidism or myxedema, for the literature in this respect shows great variation in reports as to the pathological anatomy of the heart, and it is obviously impossible to attribute to the thyroid deficiency alone the changes which are frequently reported in a condition which is accompanied by so many complicating problems as this.

From the clinical aspects of the condition there would appear to be but little doubt that the disease is brought about by chemical or physiological rather than by morphological defects, but to clear the ground and to decide certain questions in our own minds, preparatory to a broader study of the subject, we have undertaken the following brief study for the purpose of deciding whether or not the cardiac signs which appear in hypothyroidism are or are not accompanied by recognizable morphological alterations in the heart muscle. In a clinical study of a large group of hypothyroid conditions, now under way, this preliminary point appears to be of considerable importance.

For reasons of convenience, rabbits were selected for the study. The operation of thyroidectomy was very carefully performed under light ether anesthesia. Five deaths took place during or apparently as an immediate effect of the operation; these are not included in the study. All the visible thyroid tissue in the usual location was removed in each case and an attempt was made to avoid the parathyroids. As tetany did not occur in any of the 10 instances reported it seems probable that we were successful in this respect.

In each case the material removed was examined microscopically to identify absolutely the character of the tissue. In all the 10 instances reported this was found to be only an apparently normal thyroid tissue.

After operation the animals were housed and fed as carefully as possible, and were under constant observation and expert care, though no great attempt was made to study them clinically. Immediately after death, if it occurred during the laboratory hours, the heart was removed and placed in a formalin fixative. A general autopsy was made in each instance and the apparent cause of death noted. When the animal died after laboratory hours it was placed at once in the ice-chest by the laboratory orderlies and was autopsied early the next day.

The hearts were examined grossly, fixed in formalin, and sectioned in paraffin. The sections were taken in each instance through the left ventricle vertically, through the tip of both ventricles, and a third plane extended tangentially through the interventricular septum. The sections were stained with hematoxylin and eosin, and were minutely studied under the customary powers of magnification.

**EXPERIMENTS.** Rabbit No. 2. Female operated June 26. Died August 8. Duration of postoperative life forty-three days, during which time the animal exhibited the customary signs of deficient thyroid secretion. It died with a septic peritonitis and a probable general septicemia.

Microscopic examination showed practically identical lesions in all sections. The most striking alteration consisted in a definite stain attraction on the part of the cell nuclei, with in some fibers a considerable ovoid area of granular degeneration at either pole of the nucleus. In a few instances a small amount of brownish pigment was found in this area. A certain amount of parenchymatous degeneration was demonstrable in nearly all fibers. About some of the capillaries and arterioles a leukocytic infiltration had taken place in some areas associated with some evidences of proliferation of the interstitial connective-tissue cells.

Rabbit No. 3. Male. Operated June 28. Some hemorrhage took place during and after the operation, but the animal lived until July 15, seventeen days, dying apparently from a septic peritonitis.

No consistent lesions were demonstrable in the heart fibers. Occasionally a typical nuclear proliferation was seen and some cells showed moderate albuminous degeneration. The interstitial and perivascular tissues showed a few small areas of cell proliferation and of small round-cell infiltration, clearly of an acute change.

Rabbit No. 6. Male. Operated June 29. Slight oozing followed operation, but no vessels were cut. Respiration very rapid, reaching 120 per minute for about three-quarters of an hour. Died July 3, four days after the operation. At autopsy a bronchopneumonia was found, but no peritonitis or apparent wound infection. Coccidiosis of the liver was present.

Microscopic examination showed no change of a chronic nature

in any part of the heart muscle, but in a few areas, notably in the interventricular septum, there was marked congestion of the capillaries and smaller bloodvessels, with some acute parenchymatous degeneration of the muscle cells.

Rabbit No. 7. Male. Operated June 29. Slight oozing. No vessels cut. Respiration shallow and rapid, 194 per minute. Cough was at first present, but the respirations soon fell to 120 and the cough disappeared. Animal died July 2, three days after operation. No gross lesions were apparent at autopsy.

Microscopic examination showed practically no lesions present, nothing which in any way could be considered as a result of the operation or of the thyroid defect.

Rabbit No. 9. Male. Operated July 3. Died July 16, thirteen days after operation. Autopsy showed a hemorrhagic area in the mediastinum. The inferior cava was engorged. Myocardium pale, bronchopneumonia, coccidiosis of liver, with cirrhosis. Suprarenals negative.

Microscopic examination showed no lesions present.

Rabbit No. 10. Operated July 3. Died July 6, three days after operation. Autopsy showed septic pneumonia, from which a pure culture of *Bacillus coli communis* was isolated.

Microscopic examination showed no changes whatever in the heart fibers but many of the capillaries and smaller venules were packed with blood cells in which a pronounced leukocytosis was apparent. Other blood channels were filled by the growth of a *Bacillus* corresponding morphologically to the *Bacillus coli communis*.

Rabbit No. 12. Male. Operated July 14. Died July 16, two days after operation. No lesions seen at autopsy. Wound apparently in good condition.

Microscopic examination shows marked congestion of many of the capillaries and venules of the myocardium, but no changes except an occasional muscle fiber showing parenchymatous degeneration.

Rabbit No. 13. Male, operated July 14. Died July 16, two days after operation. Autopsy showed no apparent lesions. Wound in good condition.

Microscopic examination shows absolutely no changes.

Rabbit No. 14. Male. Operated July 18. Died July 25, seven days after operation. Autopsy showed no obvious lesions present.

Microscopic examination showed no lesions except occasional parenchymatous degeneration.

Rabbit No. 15. Operated July 29. Moderate hemorrhage. Died June 30, one day after operation. Abdominal wall wet, but no demonstrable peritonitis; wound moist. No peritonitis or pneumonia.

Microscopic examination of the heart showed no lesions whatever except for occasional parenchymatous degeneration.

Although the amount of material presented in this study is small and the extent of time during which the animals lived insufficient (from two to but forty-three days), since it apparently corroborates the natural conclusions derived from the clinical study of these cases, we have felt that this line of investigation is no longer profitable.

Our conclusion may be summarized as that the cardiac signs and symptoms produced as a result of hypothyroidism are not due to morphological alterations in the heart muscle, nor does this status produce secondary anatomical variations of any characteristic degree or type in the heart muscle.

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### REPORT OF CERTAIN UNUSUAL CASES OF MALARIA, WITH A BRIEF ANALYSIS OF FIFTY CASES OF THIS DISEASE.<sup>1</sup>

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DIAGNOSTIC difficulties surround the diseases with which we are not by personal experience familiar, and this applies not only to some new syndrome, but recently recognized, but with almost equal force to any condition which possibly, because of geographical location, we have been seldom or never privileged to see. Perhaps this is most true of those diseases which, once common, are now becoming, through improved hygiene, sanitation, and treatment, more and more rare and infrequent. To the younger generation of physicians this must spell unfamiliarity and diagnostic difficulty. It may be said that the more nearly a disease is stamped out the less efficient will the coming physicians be to recognize it and carry on the work of extermination. Yellow fever, smallpox, and malaria are examples which at once come to mind, and it is from this point of view that these cases are presented.

In Philadelphia today, malaria cannot be said to be common, and yet enough cases annually occur to make it very important to be on the lookout for this infection, for it is only from a human carrier that the mosquito becomes infected and a source of transmission.

During the past five years there have been admitted to the medical division of the Hospital of the University of Pennsylvania, under the care of Prof. Alfred Stengel, 58 cases, with a final diagnosis of malaria. In all but 8 of these cases the diagnosis was

<sup>1</sup> Read before the Section on General Medicine of the College of Physicians of Philadelphia, November 27, 1916.